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CARDIOPULMONARY EFFECTS OF ACUTE STRESSFUL EXERCISE AT ALTITUDE OF INDIVIDUALS WITH SICKLE CELL TRAIT (SCT)

FINAL REPORT

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U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
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A spectrum of exercise induced complications including sudden unexpected death has been reported in individuals with sickle cell trait (SCT). The etiology of these deaths and the role that sickling may play remain uncertain.

We have previously demonstrated comparable human performance to short periods of exhaustive exercise without discernible clinical differences between SCT and controls at 1270m, at simulated 2300m and after seven weeks of army basic training; (see appendix). Also we did not observe significant increases in sickling in peripheral venous blood with exercise nor with acute exposure to environmental hypoxia equivalent to 3000m. meters

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PHYSIOLOGIC RESPONSES TO ACUTE STRENUOUS EXERCISE DURING EXPOSURE TO INSPIRATORY HYPOXIA EQUIVALENT TO 4000m IN SICKLE CELL TRAIT AND CONTROLS:

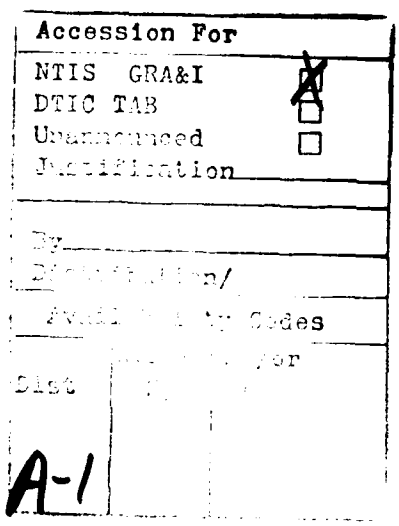
The present study was designed to study the effect of severe inspiratory hypoxia equivalent to 4000m at rest and during acute strenuous exercise in sickle cell trait subjects. Twenty seven SCT and 28 controls were exercised on a cycle ergometer to exhaustion breathing gas mixtures simulating sea level and 4000m. Cardiopulmonary variables, blood gases and percent sickling in arterial and peripheral venous blood were measured at rest and during exercise.

This study suggests that some individuals with SCT appear to be more susceptible to clinical problems during exposure and/or exercise at simulated 4000m compared to controls. Clinical symptoms precluded exercise at simulated 4000m. in 2 individuals with SCT. The cardiopulmonary and gas exchange responses to acute strenuous exercise for individuals with SCT who were able to exercise (majority) were comparable to controls under both experimental conditions. Lower extremity exercise does not appear to significantly increase sickling in venous blood of non-exercising limbs. One minute post-exercise sickling remains elevated despite a significant increase in SvO2 which would suggest release of sickled red cells from the microcirculation of tissue not actively involved during exercise. The practical absence of sickling in arterial blood probably reflects the rapid reversibility of sickled cells as they traverse the better oxygenated pulmonary capillaries. The ready reversibility and sickling kinetics of HbAS containing sickled cells may explain why sickling does not appear to modulate exercise performance under these experimental conditions. No physiologic parameter clearly distinguishes individuals with SCT who are more likely to experience clinical symptoms than those who are asymptomatic during exercise and/or exposure to inspiratory hypoxia

FOREWORD

Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

For the protection of human subjectds the investigators have adhered to policies of applicable Federal Law 45CFR46.



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PRELIMINARY COMMENTS

Our research initiative has included a stepwise phased series of studies in which the cadiopulmonary, gas exchange, and hematologic responses to acute strenuous exercise were evaluated under varying levels of environmental hypoxia. The results of the studies performed at 1270m, simulated sea level, simulated 2300m, and after seven weeks of army basic training have already been published in peer review journals (see appendix). The results of the present report, at simulated 4000m, are being prepared in manuscript form for submission to peer review scientific journals.

As a result of the removal of all occupational disqualifications for individuals with SCT in January 1985, there remains a genuine need for scientifically valid data in order to establish appropriate policy decisions for active duty military individuals with SCT so that the success of military missions will not be endangered. Our recent data at simulated 4000m suggests that populations of symptomatic and asymptomatic individuals may be able to be identified. Characterization of these groups may ultimately lead to the identification of a sub-population of individuals with SCT who may be at increased risk for exertion related medical complications and SUD. Further studies, including an endurance exercise study remain necessary to perform in order to solve these complex questions.

At the same time that the sickle cell trait studies were performed, we also collected interesting physiological data on exercise performance under hypoxic conditions in healthy black individuals. This data is being analyzed and prepared for publication.

PHYSIOLOGIC RESPONSES TO ACUTE STRENUOUS EXERCISE DURING EXPOSURE TO INSPIRATORY HYPOXIA EQUIVALENT TO 4000m IN SICKLE CELL TRAIT AND CONTROLS

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SPECIFIC AIMS

1) TO DETERMINE WHETHER DISCERNIBLE CLINICAL DIFFERENCES WOULD BE OBSERVED BETWEEN SCT AND CONTROLS AT REST AND DURING EXERCISE WHILE EXPOSED TO A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m.

2) TO DETERMINE THE CARDIOPULMONARY PERFORMANCE OF INDIVIDUALS WITH SCT TO ACUTE STRENUOUS EXERCISE COMPARED TO CONTROLS UNDER CONDITIONS OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m, and SIMULATED SEA LEVEL.

3) TO EVALUATE WHETHER SUBTLE PHYSIOLOGIC ABNORMALITIES, ALTHOUGH CLINICALLY INAPPARENT, MIGHT BE PRESENT IN SCT.

4) TO DETERMINE THE EFFECTS THAT EXERCISE AND/OR EXPOSURE TO INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m WOULD HAVE ON PERCENT SICKLING.

5) TO DETERMINE WHETHER PERCENT SICKLING AND %HBS CORRELATE WITH PARAMETERS OF EXERCISE PERFORMANCE AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m.

PROTOCOL DAY 1

- - - 58 HEALTHY, BLACK MALE BASIC TRAINEE VOLUNTEERS PARTICIPATED IN THIS PHASE OF OUR STUDY.

- - - THE SELECTION PROCESS HAS BEEN PREVIOUSLY DISCUSSED.

- - - 30 WITH ELECTROPHORETIC PATTERNS CONSISTENT WITH HbAS (SCT) AND 28 CONTROLS.

- - - VOLUNTEERS WERE RANDOMLY SELECTED FROM AMONG GROUPS OF AVAILABLE SCT AND CONTROL VOLUNTEERS. ALL VOLUNTEERS SIGNED INFORMED CONSENT.

--- ALL VOLUNTEERS HAD AN UNREMARKABLE PAST MEDICAL HISTORY, WERE NONSMOKERS, AND FREE OF INTERMITTENT ILLNESS.

--- ALL RECEIVED A PHYSICAL EXAMINATION, EKG, CXR, PFTs, AND U/A.

- - - THE EXERCISE PROTOCOL INVOLVED TWO DAYS, AND WAS PERFORMED IN EL PASO, TEXAS, WHERE THE P_B = 656 mmHg. VOLUNTEERS UNDERWENT AN EXERCISE FAMILIARIZATION SESSION IN OUR EXERCISE LABORATORY.

--- ON DAY 1, EACH VOLUNTEER PERFORMED TWO INCREMENTAL EXERCISE TESTS TO EXHAUSTION WHILE BREATHING THROUGH A MOUTHPIECE HUMIDIFIED GAS MIXTURES, WHICH WERE RANDOMLY ASSIGNED EITHER 14% F_IO_2 (P_IO_2 = 85 mmHg) OR 24% F_IO_2 (P_IO_2 = 146 mmHg) EQUIVALENT TO 4000m AND SEA LEVEL CONDITIONS, RESPECTIVELY. GAS MIXTURES WERE ASSIGNED IN A SINGLE BLIND FASHION. EXERCISE WAS PERFORMED AFTER TWO HOURS OF EQUILIBRATION, BREATHING THESE SAME GAS MIXTURES THROUGH A RESPIRATORY MASK. A TWO-HOUR REST PERIOD BETWEEN INCREMENTAL EXERCISE TESTS WAS ALLOWED. THE SECOND GAS MIXTURE NOT USED IN THE MORNING WAS USED IN THE AFTERNOON.

EXERCISE TESTING

EXERCISE TESTING WAS PERFORMED UTILIZING AN ELECTRONICALLY BRAKED CYCLE ERGOMETER WITH THE WORKLOAD INCREASING AT 25 WATT INTERVALS PER MINUTE. PRIOR TO EXERCISE, THE VOLUNTEERS WERE CHANGED OVER TO A TWO-WAY RESPIRATORY VALUE (HONS-RUDOLPH MODEL 2700) WHILE CONTINUING TO BREATHE THE SAME GAS CONCENTRATION UNTIL COMPLETING THE EXERCISE TEST. A MCG-2000 EXERCISE SYSTEM WHICH INTERFACED TO A PERKIN-ELMER MASS SPECTROMETER WAS USED. OXYGEN CONSUMPTION, CO_2 PRODUCTION AND MINUTE VENTILATION WERE MONITORED IN A BREATH-BY-BREATH FASHION.

CONTINUOUS MONITORING OF HR AND 12-LEAD EKG OCCURRED.

BP WAS CONTINUOUSLY MONITORED ELECTRONICALLY UTILIZING AN INFRASOUND 4000.

OXYGEN SATURATION WAS MONITORED CONTINUOUSLY BY BOTH HP AND BIOX II EAR OXIMETERS.

ARTERIAL BLOOD GAS ANALYSIS WAS PERFORMED IN DUPLICATE, UTILIZING TWO IL-1300 MACHINES WITH TONOMETRIC CORROBORATION (MORQUEST).

PROTOCOL - DAY 2

- - ON DAY 2, TWO SSETS WERE PERFORMED BY EACH VOLUNTEER WHILE BREATHING GAS MIXTURES OF EITHER 14% OR 24% F_IO_2 AFTER TWO HOURS OF EQUILIBRATION AT EACH RESPECTIVE GAS MIXTURE. THE SSET AT 14% F_I0_2 OCCURRED AT TWO LEVELS -- 50% AND 70% OF THE MAXIMUM POWER ACHIEVED DURING THE IET-14%. THE SSET AT 24% OCCURRED AT THREE LEVELS, WITH THE THIRD LEVEL OCCURRING AT 70% OF THE MAXIMUM POWER ACHIEVED DURING THE IET-24%.

- - BASELINE ANTECUBITAL VENOUS BLOOD WAS OBTAINED FOR BOTH AEROBIC AND ANAEROBIC MEASUREMENTS. AEROBIC DETERMINATIONS INCLUDED A HEMOGRAM, 2, 3DPG, P_{50} HAPTOGLOBIN, SMA-20, Posm LACTIC ACID. ANAEROBIC SAMPLES WERE OBTAINED FOR BLOOD GASES AND %S. A BRACHIAL VENOUS CATHETER WAS INSERTED IN 11 VOLUNTEERS WITH SCT FOR EXERCISE %S AND VENOUS BLOOD GASES. TWELVE CONTROLS HAD BRACHIAL VENOUS CATHETERS FOR VBGs.

- - A RADIAL ARTERIAL LINE WAS INSERTED PRIOR TO THE EXERCISE AND ARTERIAL BLOOD GAS SAMPLES WERE OBTAINED FOR %S AND aBgs DURING EACH LEVEL OF THE STEADY STATE EXERCISE AS INDICATED BY THE ARROWS. A TWO-HOUR REST PERIOD BETWEEN THE TWO SSETS WAS ALLOWED.

- - A HEMOGRAM, SMA-20, LACTIC ACID AND Posm WERE OBTAINED ONE MINUTE POST-CESSATION OF EXERCISE WHILE STILL BREATHING THE GAS MIXTURE.

- - A 24-HOUR URINE FOR MYOGLOBIN BY RIA WAS OBTAINED ON ALL VOLUNTEERS.

- - A SERIES OF CLINICAL QUESTIONS AS MODIFIED FROM THE ENVIRONMENTAL SYSTEMS QUESTIONNAIRE (ESQ) WERE GIVEN TO ALL VOLUNTEERS DURING EXPOSURE TO BOTH 14% AND 24% GAS MIXTURES AND AT THE COMPLETION OF EXERCISE AT BOTH OF THESE CONDITIONS.

ANTHROPOMETRIC AND PULMONARY FUNCTION MEASUREMENTS OF HEALTHY BLACK MALES WITH SCT AND CONTROLS

(mean ± SEM)

	SCT (n = 30)	Controls (n = 28)
Age (yr)	19 ± 0.2*	20 ± 0.3*
Height (cm)	176 ± 1.2	177 ± 1.6
Weight (kg)	75 ± 1.7	77 ± 1.9
FVC (L)	4.85 ± .10	5.18 ± .14
FEV_1 (L)	4.19 ± .08	4.38 ± .11
FEV_1/FVC	86 ± 0.9	85 ± 1.1
TLC (L)	6.03 ± .14	6.38 ± .19
DL_{CO} (ml/min/mmHg)	37.2 ± 1.1	37.9 ± 0.9
DL/V_A	6.34 ± .18	6.29 ± .14

*significant difference between groups by t-test at $p < 0.05$

ANTHROPOMETRIC AND PFT CHARACTERISTICS

THIS TABLE DEMONSTRATES THE ANTHROPOMETRIC AND PFT CHARACTERISTICS OF OUR STUDY GROUPS.

ALL RESULTS ARE EXPRESSED AS MEAN ± SEM.

THERE WAS A SMALL, BUT STATISTICALLY SIGNIFICANT DIFFERENCE FOR AGE BETWEEN THE SCT AND CONTROL GROUPS. THIS DIFFERENCE IS OF TRULY DOUBTFUL CLINICAL SIGNIFICANCE.

NO DIFFERENCES WERE OBSERVED FOR HEIGHT AND WEIGHT BETWEEN THE TWO GROUPS.

PULMONARY FUNCTION DATA REVEALED NO DIFFERENCES IN FLOWS, VOLUMES, AND SINGLE BREATH DIFFUSING CAPACITIES (D_LCO) BETWEEN THE TWO GROUPS.

HEMATOLOGICAL VALUES OF SCT AND CONTROLS

(mean ± SEM)

	Hb (g/dl)	Hct (%)	RBC (mill/ul)	MCV (fl)	MCH (uug)	MCHC (%)
SCT	13.9 ± .2	42.3 ± .6	4.92 ± .07	86.0 ± 1.0	28.3 ± .3	32.9 ± .2
Controls	14.2 ± .2	42.8 ± .6	4.96 ± .09	86.4 ± 0.9	28.8 ± .4	33.3 ± .2

*significant difference between groups by t-test at $p < 0.05$

SPECIAL HEMATOLOGY TESTS OF SCT AND CONTROLS

	SCT		CONTROLS	
	mean ± SEM	Range	mean ± SEM	Range
HbS (% major Hb)	40.2 ± 0.4	35.8 - 43.8	---	---
2,3 DPG (umol/L)	2.4 ± .06	1.5 - 3.1	2.3 ± .05	1.8 - 2.7
P_{50} (mmHg)	27.7 ± .2	25 - 29.5	27.2 ± .3	23 - 30
Hapto. (mg/dl)	51 ± 7.3	5 - 120	72 ± 8.6	5 -166

*Significant difference between groups by t test at $p < 0.05$.

HEMATOLOGY VALUES FOR SCT AND CONTROLS

THIS TABLE DEMONSTRATES THAT BOTH GROUPS POSSESSED COMPARABLE VALUES FOR HB, HCT, RBC COUNT, AND RED BLOOD CELL INDICES.

SPECIAL HEMATOLOGY VALUES

THIS TABLE DEMONSTRATES THE RESULTS OF SOME SPECIAL HEMATOLOGY TESTS PERFORMED AT REST IN BOTH SCT AND CONTROL VOLUNTEERS AT SIMULATED SEA LEVEL.

VALUES FOR P_{50} AND 2,3DPG WERE WNL, COMPARABLE, AND NOT SIGNIFICANTLY DIFFERENT BETWEEN THE TWO GROUPS.

THE %HbS IN THE SCT GROUP WAS 40.2 ± 0.4 EXPRESSED AS $X \pm SEM$ WITH A RANGE OF 35.8-43.8. THESE VALUES ARE CONSISTENT WITH THOSE AVAILABLE IN THE LITERATURE AND THOSE PREVIOUSLY REPORTED BY US, AND REPRESENT THE VALUES OBTAINED FROM OUR Hb REFERENCE LABORATORY AT BAYLOR UNIVERSITY, DALLAS, TEXAS.

CLINICAL SYMPTOMS

- AS INDICATED PREVIOUSLY, ALL PARTICIPANTS WERE ASKED TO RESPOND TO A SERIES OF QUESTIONS MODIFIED FROM THE ENVIRONMENT SYSTEMS QUESTIONNAIRE DURING EXPOSURE TO THE 14% AND 24% GAS MIXTURES AS WELL AS AFTER EXERCISE AT EACH OF THESE CONDITIONS. IN ADDITION, SYMPTOMATIC COMPLAINTS SPONTANEOUSLY OFFERED BY THE PARTICIPANTS WERE NOTED.
- ALTHOUGH THE POSSIBILITY EXISTED FOR AMS, HAPE, AND HACE, THE LIKELIHOOD OF SUCH PHENOMENA OCCURRING WERE REMOTE BECAUSE OF THE SHORT DURATION OF EXPOSURE TO HYPOXIA. SXS OF ACUTE EXPOSURE TO HYPOXIA WOULD HAVE BEEN MORE LIKELY.
- CLINICAL SXS WERE GROUPED INTO FOUR MAJOR AREAS BASED ON VOLUNTEER RESPONSES:
  1. SYMPTOM COMPLEX OF H, D.L
  2. LEG CRAMPS
  3. ABDOMINAL PAIN -CRAMPS/LUQ PAIN
  4. CHEST PAIN

  DISCERNIBLE DIFFERENCE IN CLINICAL SYMPTOMS BETWEEN SCT AND CONTROLS WAS NOTED.
- 22 INSTANCES OF CLINICAL SYMPTOMS WERE NOTED IN 12 INDIVIDUALS WITH SCT FROM THE GROUP OF 30 SCT VOLUNTEERS.
- 8 INSTANCES OF CLINICAL SYMPTOMS WERE NOTED IN 5 CONTROLS OF THE 28 VOLUNTEERS.
- CLINICAL SYMPTOMS PRECLUDED EXERCISE TESTING THREE INDIVIDUALS WITH SCT: TWO SCT VOLUNTEERS AT 14% EXPOSURE AND ONE AT 24%. ONE INDIVIDUAL IN THE SCT GROUP WAS ABLE TO EXERCISE AT 24%-2X AND UNABLE TO EXERCISE ON 14%-2X.
- ALTHOUGH THE CONTROL GROUP EXPERIENCED SYMPTOMS, ESPECIALLY AT 14%, CLINICAL SYMPTOMS DID NOT PRECLUDE EXERCISE TESTING IN ANY OF THE CONTROLS. FOUR OF EIGHT INSTANCES OF COMPLAINTS IN CONTROLS RELATED TO H, D, LIGHT HEADEDNESS.
- ABDOMINAL PAIN, IN PARTICULAR LUQ PAIN, OCCURRED ONLY IN THE SCT GROUP. THE THREE INDIVIDUAL WITH LUQ PAIN WERE ABLE TO SUCCESSFULLY COMPLETE EXERCISE. REPEAT EXPOSURE ON THE FOLLOWING DAY TO 14% ELICITED REPEAT LUQ PAIN IN TWO OF THREE INDIVIDUALS.
- - THE EXERCISE DATA THAT WILL BE PRESENTED REPRESENTS DATA FROM ALL OF THE CONTROLS AND THOSE INDIVIDUALS WITH SCT WHO WERE ABLE TO EXERCISE.

CARDIOPULMONARY PERFORMANCE OF SCT (n = 27) AND CONTROLS (n = 28) DURING INCREMENTAL EXERCISE AT A LEVEL OF P_IO_2 EQUIVALENT TO SEA LEVEL (mean ± SEM)

	Rest		Peak Exercise			
	SCT	Controls	SCT	% Pred	Controls	% Pred
Power (W)			256± 7	98	268± 6	105
$\dot{V}O_2$ (L/min)	.42± .02	.42±.02	3.29±.09	96	3.46±.10	101
$\dot{V}O_2$/kg (ml/min/kg)	5.7± .2	5.4± .3	44.5±1.0		44.6±1.1	
$\dot{V}CO_2$ (L/min)	.38± .01	.39±.02	4.10±.12		4.33±.12	
$\dot{V}_E$ (L/min)	16.2± .7	16.2± .8	134± 9		145± 4	
R	.91± .02	.92±.02	1.25±.01		1.26±.01	
HR (bpm)	83± 2	81± 2	192± 2	97	189± 2	96
O_2 Pulse (ml/beat)	5.2± .3	5.0± .3	17.1± .4		18.3± .6	
AT ($\dot{V}O_2$, L/min)			1.78±.07		1.74±.07	

*Significant difference between groups by repeated measures ANOVA at $p < 0.05$.

IET AT SSL

THIS TABLE DEMONSTRATES THE CARDIOPULMONARY RESPONSE TO INCREMENTAL EXERCISE AT A LEVEL OF P_IO_2 EQUIVALENT TO SEA LEVEL FOR SCT (n = 27) AND CONTROLS (n = 28).

THE DATA AT REST AND AT PEAK EXERCISE ARE SHOWN AND EXPRESSED AS ($\bar{X} \pm$ SEM).

AT REST, NO STATISTICALLY SIGNIFICANT DIFFERENCES WERE OBSERVED BETWEEN THE CONTROL AND SCT GROUPS FOR HR, $\dot{V}_E$, $\dot{V}O_2$, $\dot{V}CO_2$, R AND O_2 PULSE.

AT PEAK INCREMENTAL EXERCISE, A SIMILAR RESPONSE WAS OBSERVED BETWEEN THE SCT AND CONTROL GROUPS FOR THE FOLLOWING PARAMETERS: POWER ACHIEVED, HR, $\dot{V}_E$, $\dot{V}O_2$, R, O_2 PULSE AND ANAEROBIC THRESHOLD.

THE GROUPS ACHIEVED 95 AND 105% OF THE PREDICTED VALUE FOR POWER, 96% AND 101% PREDICTED VALUES FOR VO_2 AND 97% AND 96% OF THE PREDICTED VALUES FOR HR FOR THE SCT AND CONTROL GROUPS, RESPECTIVELY.

CARDIOPULMONARY PERFORMANCE OF SCT (n = 27) AND CONTROLS (n = 28) DURING INCREMENTAL EXERCISE AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000m (mean ± SEM)

	Rest		Peak Exercise			
	SCT	Controls	SCT	% Pred	Controls	% Pred
Power (W)			205± 6	79	208± 6	81
$\dot{V}O_2$ (L/min)	.46± .02	.44±.02	2.46±.06	72	2.58±.07	76
$\dot{V}O_2$/kg (ml/min/kg)	6.2± .2	5.7± .3	33.2± .7		33.6± .8	
$\dot{V}CO_2$ (L/min)	.40± .02	.40±.01	3.16±.09		3.28±.09	
$\dot{V}_E$ (L/min)	17.7± .7	17.2± .6	130± 3		133± 4	
R	.88± .01	.88±.01	1.30±.01		1.27±.01	
HR (bpm)	90± 3	88± 3	184± 2	93	181± 2	92
O_2 Pulse (ml/beat)	5.1± .2	5.0± .2	13.3± .3		14.3± .4	
AT ($\dot{V}O_2$, L/min)			1.43±.05		1.45±.05	

*Significant difference between groups by repeated measures ANOVA at $p < 0.05$.

IET AT S4000m

THIS TABLE IS SIMILAR TO THE PREVIOUS TABLE, BUT SHOWS THE CARDIOPULMONARY RESPONSE TO INCREMENTAL EXERCISE AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000m FOR SCT (n = 27) AND CONTROLS (n = 28).

RESULTS AT REST AND AT PEAK EXERCISE ARE SHOWN AND EXPRESSED AS $\bar{X} \pm$ SEM.

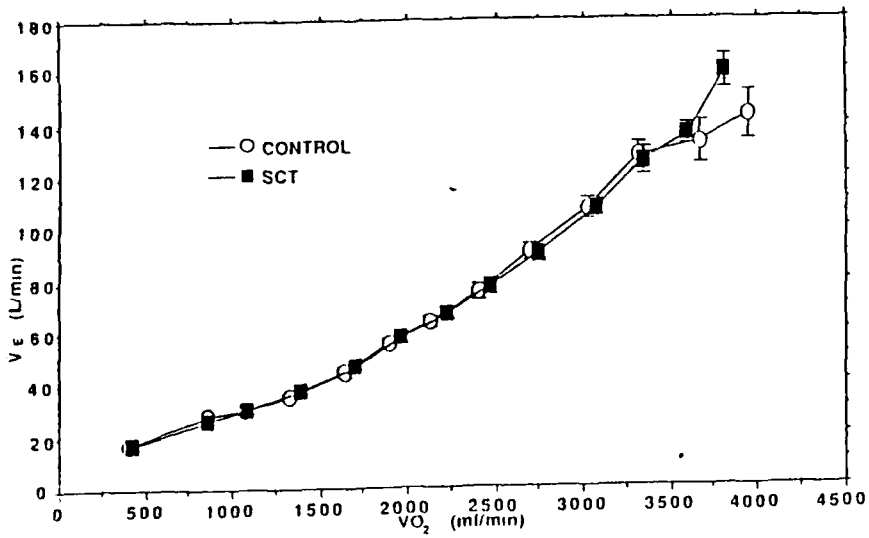
NO STATISTICALLY SIGNIFICANT DIFFERENCES WERE NOTED AT REST BETWEEN THE CONTROL AND SCT GROUPS FOR THE SAME PREVIOUSLY MENTIONED PARAMETERS.

AGAIN, NO STATISTICALLY SIGNIFICANT DIFFERENCES WERE NOTED AT PEAK EXERCISE BETWEEN THE SCT AND CONTROL GROUPS.

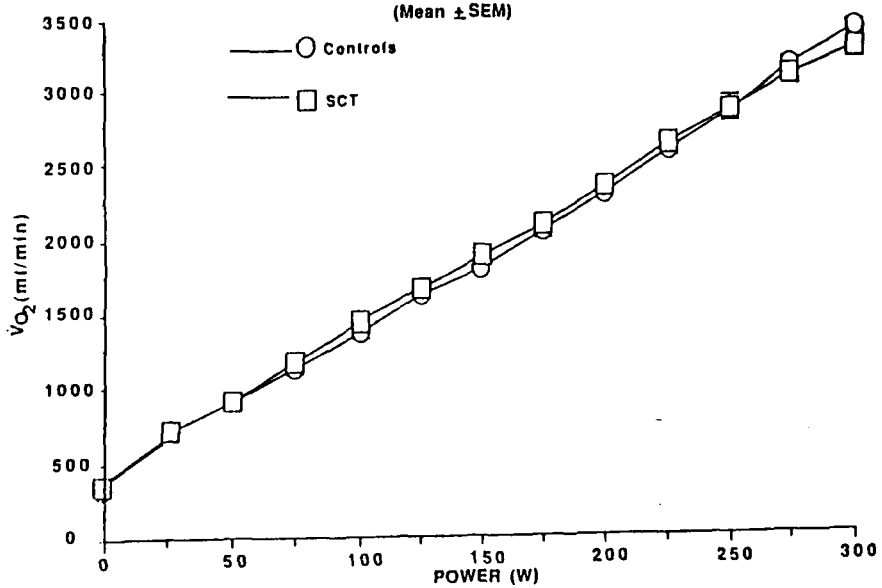
FURTHERMORE, IT SHOULD BE NOTED THAT THE DECREMENT IN EXERCISE PERFORMANCE BETWEEN THE TWO GROUPS FOR THE FOLLOWING PARAMETERS: POWER, HR AND $\dot{V}O_2$ WERE COMPARABLE FOR BOTH GROUPS AND CONSISTENT WITH PREVIOUS HYPOBARIC HYPOXIA EXERCISE STUDIES.

		SCT	CONTROL
POWER	(Δ%)	19%	24%
$\dot{V}O_2$		24%	25%
HR		4%	4%

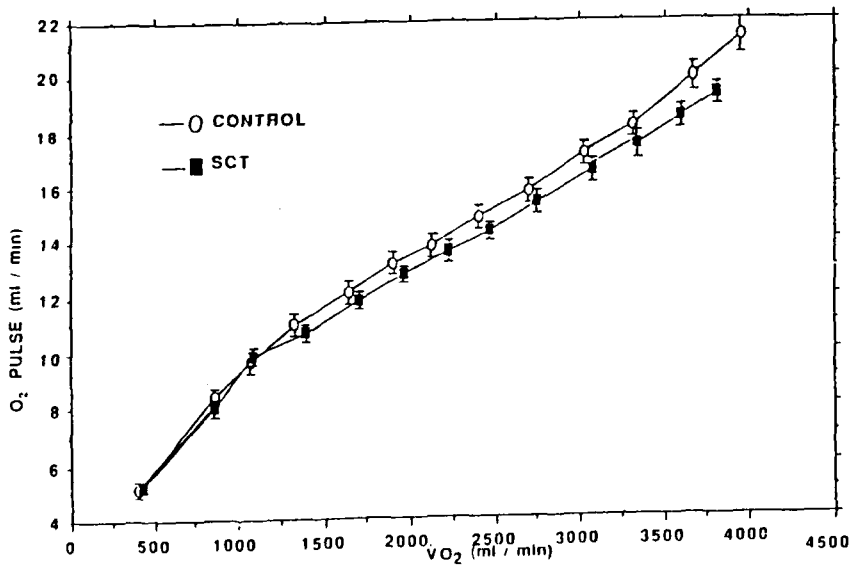
THE RELATIONSHIP OF $\dot{V}_E$ WITH $\dot{V}O_2$
DURING INCREMENTAL EXERCISE AT A LEVEL OF P_IO_2
EQUIVALENT TO SEA LEVEL IN SCT (n=30) AND CONTROLS (n=28)
(Mean ±SEM)



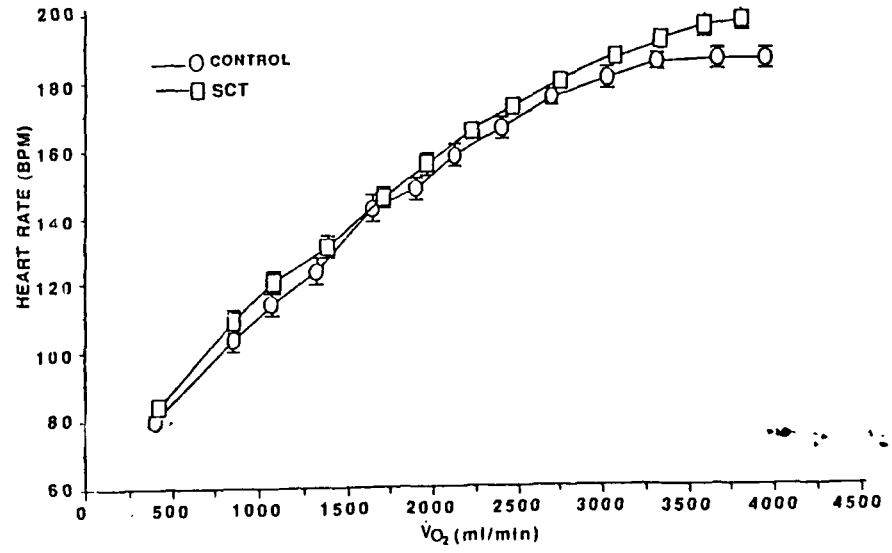
THE RELATIONSHIP OF POWER WITH $\dot{V}O_2$
DURING INCREMENTAL EXERCISE AT A LEVEL OF P_IO_2
EQUIVALENT TO SEA LEVEL IN SCT (n=30) AND CONTROLS (n=28)
(Mean ±SEM)



THE RELATIONSHIP OF O_2 PULSE WITH $\dot{V}O_2$
DURING INCREMENTAL EXERCISE AT A LEVEL OF P_IO_2
EQUIVALENT TO SEA LEVEL IN SCT (n=30) AND CONTROLS (n=28)
(Mean ± SEM)



THE RELATIONSHIP OF HEART RATE WITH $\dot{V}O_2$
DURING INCREMENTAL EXERCISE AT A LEVEL OF P_IO_2
EQUIVALENT TO SEA LEVEL IN SCT (n=30) AND CONTROLS (n=28)
(Mean± SEM)

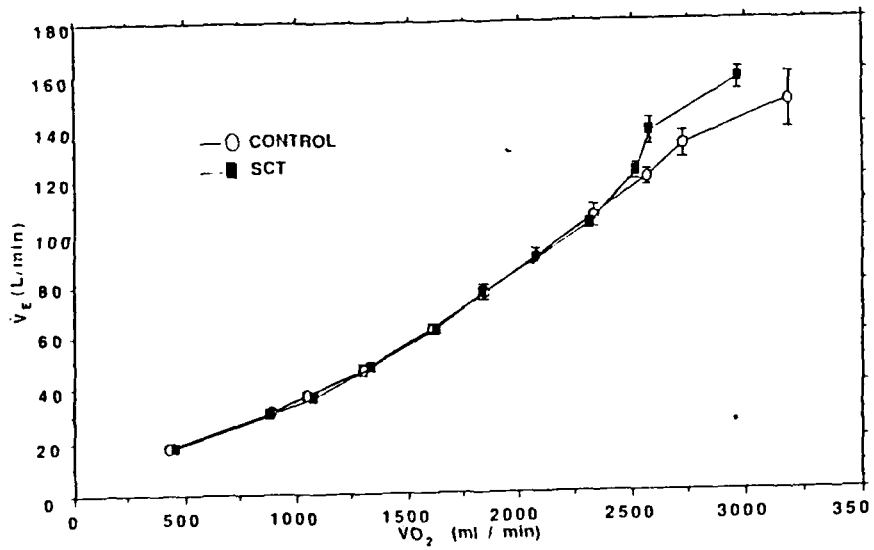


IET TRENDING - SSL

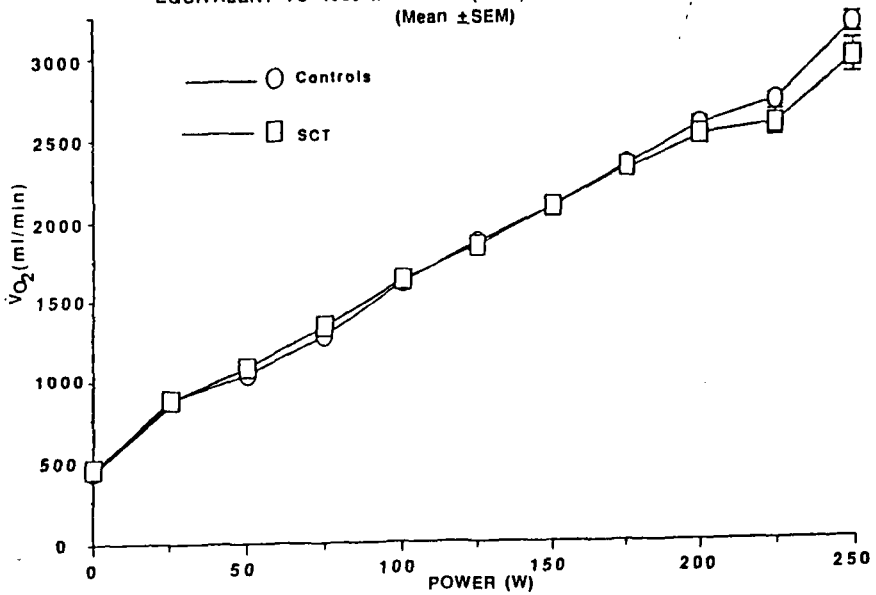
THIS FIGURE GRAPHICALLY DEMONSTRATES IN FOUR PANELS THE RELATIONSHIP BETWEEN POWER AND OXYGEN CONSUMPTION, $\dot{V}_E$ AND OXYGEN CONSUMPTION, HR AND OXYGEN CONSUMPTION, AND O_2 PULSE AND OXYGEN CONSUMPTION FOR EACH GROUP THROUGHOUT THE INCREMENTAL EXERCISE TEST AT SIMULATED SEA LEVEL. THE CIRCLES DESIGNATE THE CONTROLS AND THE BOXES THE SCT.

WHEN THE DATA ARE DISPLAYED IN THIS FASHION, THE COMPARABILITY OF EXERCISE PERFORMANCE BETWEEN THE SCT AND CONTROL GROUPS THROUGHOUT EXERCISE AT SIMULATED SEA LEVEL IS FURTHER REINFORCED.

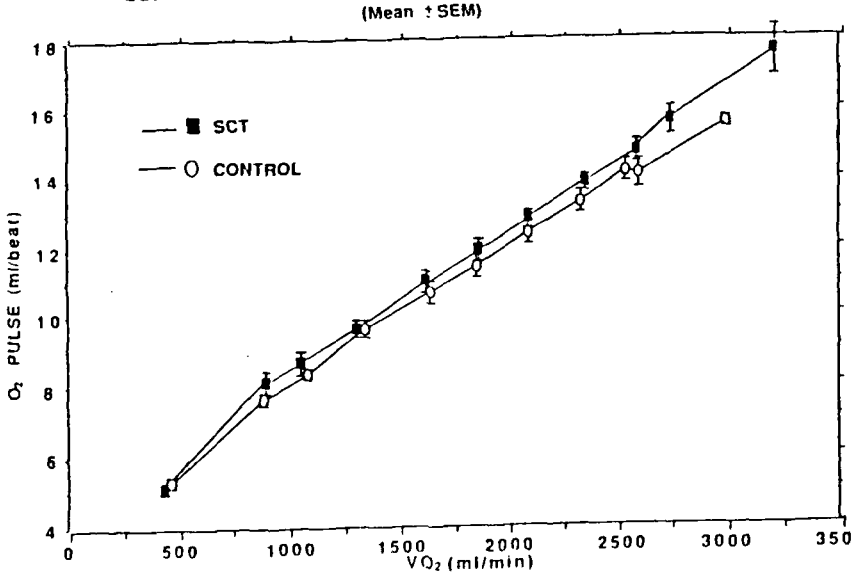
THE RELATIONSHIP OF $\dot{V}_E$ WITH $\dot{V}O_2$
DURING INCREMENTAL EXERCISE AT A LEVEL OF INSPIRATORY HYPOXIA
EQUIVALENT TO 4000 M IN SCT (n=30) AND CONTROLS (n=28)
(Mean ± SEM)



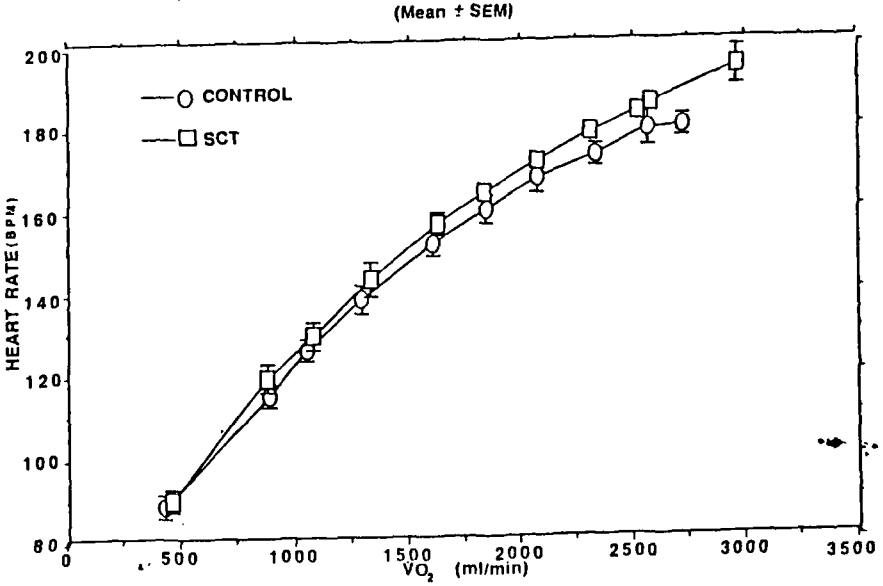
THE RELATIONSHIP OF POWER WITH $\dot{V}O_2$
DURING INCREMENTAL EXERCISE AT A LEVEL OF INSPIRATORY HYPOXIA
EQUIVALENT TO 4000 m IN SCT (n=30) AND CONTROLS (n=28)
(Mean ±SEM)



THE RELATIONSHIP OF O_2 PULSE WITH $\dot{V}O_2$
DURING INCREMENTAL EXERCISE AT A LEVEL OF INSPIRATORY HYPOXIA
EQUIVALENT TO 4000 M IN SCT (n=30) AND CONTROLS (n=28)
(Mean ± SEM)



THE RELATIONSHIP OF HEART RATE WITH $\dot{V}O_2$
DURING INCREMENTAL EXERCISE AT A LEVEL OF P_IO_2
EQUIVALENT TO 4000 M IN SCT (n=30) AND CONTROLS (n=28)
(Mean ± SEM)



IET TRENDING - S4000m

LIKEWISE, THIS FIGURE WHICH IS SIMILAR TO THE PREVIOUS ONE, SHOWS THE DATA FROM A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000m. THE CIRCLES DESIGNATE THE CONTROLS AND THE BOXES THE SCT GROUP. AGAIN, THESE GRAPHS REINFORCE THE COMPARABILITY OF EXERCISE PERFORMANCE THROUGHOUT THE IET AT S4000m FOR BOTH GROUPS.

GAS EXCHANGE OF SCT (n=23) AND CONTROLS (n=21)
DURING STEADY STATE EXERCISE TEST (SS) AT A LEVEL
OF P_IO_2 EQUIVALENT TO SEA LEVEL (mean ± SEM)

	REST		SSI		SSII		SSIII	
	SCT	CONTROLS	SCT	CONTROLS	SCT	CONTROLS	SCT	CONTROLS
Power			104±3	108±3	147±5	151±4	183±4	189±5
%$\dot{V}O_2$ Peak at 24%			62	60	80	76	94	91
PaO_2 (mmHg)	99±0.9	97±1.3	100±1.2	103±1.3	96±1.3	97±1.4	95±1.3	96±1.5
$PaCO_2$ (mmHg)	40±0.5	407±0.6	39±0.6	38±0.6	37±0.6	36±0.8	33±0.5	33±0.8
pH	7.39±.00	7.37±.00	7.35±.00	7.35±.00	7.34±.01	7.33±.01	7.31±.01	7.31±.01
SaO_2 (%)	97±0.2	96±0.2	97±0.2	97±0.2	96±0.2	96±0.2	96±0.2	97±0.2
P (A-a)O2 (mmHg)	3±0.7	5±0.9	8±1.1	7±0.8	16±1.3	15±1.3	21±1.4	20±1.2
V_D/V_T (%)	31±1.0	33±1.2	18±0.9	18±0.8	16±0.9	16±0.8	15±0.7	16±0.6

*Significant difference between groups by repeated measures ANOVA at $p < 0.05$.

GAS EXCHANGE AT SSL DURING SSET

THE GAS EXCHANGE DATA MEASURED AT REST AND AT LEVELS I, II, AND III OF THE STEADY STATE EXERCISE TEST PERFORMED AT SIMULATED SEA LEVEL IS REPRESENTED IN THIS TABLE FOR SCT (n = 23) AND CONTROLS (n = 21).

THE RESULTS ARE EXPRESSED AS $\overline{X} \pm$ SEM.

AT REST, NO STATISTICALLY SIGNIFICANT DIFFERENCES WERE NOTED IN THE FOLLOWING PARAMETERS BETWEEN THE TWO GROUPS: SaO_2, PaO_2, $PaCO_2$, pH, $P(A\text{-}a)O_2$, and V_D/V_T.

LIKEWISE, NO STATISTICALLY SIGNIFICANT DIFFERENCES IN GAS EXCHANGE PARAMETERS DURING STEADY STATE LEVELS I, II, II CONDITIONS AT A COMPARABLE POWER AND $\dot{V}O_2$ WERE NOTED BETWEEN THE SCT AND CONTROL GROUPS.

GAS EXCHANGE OF SCT (n = 19) AND CONTROLS (n = 21)
DURING STEADY STATE TEST AT A LEVEL
OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000m (mean + SEM)

	REST		SSI		SSII	
	SCT	CONTROLS	SCT	CONTROLS	SCT	CONTROL
Power			104±3	108±3	146±5	151±4
%$\dot{V}O_2$ Peak at 14%			81	81	98	98
PaO_2 (mmHg)	45±1.0	46±1.1	42±0.7	42±0.8	43±0.8	42±0.9
$PaCO_2$ (mmHg)	37±0.5	37±0.7	31±0.4	30±0.8	28±0.5	27±0.7
pH	7.41±.00	7.41±.00	7.40±.01	7.41±.00	7.35±.01	7.37±.01
SaO_2 (%)	80±1.3	81±1.1	76±0.9	78±1.1	75±0.8	75±1.2
P (A-a)O2 (mmHg)	2±0.6	2±0.5	16±0.7	17±0.6	20±0.8	21±0.8
V_D/V_T (%)	29±1.0	31±0.9	20±0.7	20±0.8	21±0.8	20±0.9

*Significant difference between groups by repeated measures ANOVA at $p < 0.05$.

GAS EXCHANGE - 4000m

THIS TABLE IS SIMILAR TO THE PRECEDING ONE AND REVEALS GAS EXCHANGE RESULTS FOR BOTH GROUPS AT REST AND DURING SSET AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000m.

AT REST FOR THE SAME GAS EXCHANGE PARAMETERS MENTIONED ON THE PREVIOUS SLIDE, NO STATISTICALLY SIGNIFICANT DIFFERENCES BETWEEN THE SCT AND CONTROL GROUPS WERE NOTED.

DURING STEADY STATE LEVEL II FOR COMPARABLE POWER AND Vo_2 NO STATISTICALLY SIGNIFICANT DIFFERENCES BETWEEN THE TWO GROUPS WERE NOTED IN THE FOLLOWING GAS EXCHANGE PARAMETERS: SaO_2, PaO_2, pH, $P(A\text{-}a)O_2$ and V_D/V_T.

IT SHOULD BE NOTED THAT THE INCREASE IN THE $P\ (A\text{-}a)O_1$ WITH SSII-14% WAS COMPARABLE WITH THAT NOTED AT SSET LEVEL III AT 24% BEING APPROXIMATELY 20-21 IN EACH CASE. THE INCREASE IN THE $(P\text{-}A\text{-}a)O_2$ IS COMPARABLE WITH THAT WHICH HAS BEEN PREVIOUSLY REPORTED IN THE LITERATURE DURING HYPOBARIC HYP0XIA OF 4000m.

% SICKLING

PERCENT SICKLING (%S) WAS DEFINED AS THE NUMBER OF SICKLED CELLS EXPRESSED AS A PERCENT OF 500 RED BLOOD CELLS COUNTED ON A WET MOUNTED SEALED SLIDE OF BLOOD FIXED IN 1% GLUTARALDEHYDE PHOSPHATE BUFFER SOLUTION. PHASE CONTRAST PHOTOGRAPHS OF THESE WET MOUNT PREPARATIONS WERE EVALUATED BY TWO OBSERVERS.

% SICKLING AND VENOUS BLOOD GASES IN SCT(n=11) AND CONTROLS (n=12) DURING LEVELS OF P_IO_2 EQUIVALENTS TO SEA LEVEL AND 4000m (Mean ±SEM)

	SCT			CONTROLS		
	Baseline	Peak	Post	Baseline	Peak	Post
SIM. SEA LEVEL						
% SICKLING(%)	0.4±0.1	0.8±0.4	0.7±0.4			
P_VO_2(mmHg)	32±2.3	42±5.0	57±7.6	33±2.1	47±4.9	67±4.8
S_VO_2(%)	54±5.1	62±8.7	77±6.0	56±4.1	69±5.7	86±3.5
pH	7.33±.01	7.23±.02	7.23±.02	7.32±.01	7.27±.01	7.25±0.2
SIM. 4000m						
% SICKLING(%)	0.8±0.3	9.3±2.9	10.0±3.5			
P_VO_2(mmHg)	25±1.6	19±2.6	27±4.0	25±2.5	20±1.5	32±3.1
S_VO_2(%)	39±3.8	24±5.3	39±7.5	40±5.8	27±4.2	47±6.6
pH	7.35±.01	7.26±.02	7.22±.02	7.35±.01	7.28±.01	7.24±.02

VBGs AND %S AT SSL + S4000m
DATA IS PRESENTED AS ($\bar{X}$ + SEM)

- - THIS TABLE DEMONSTRATES THE % SICKLING AND VENOUS BLOOD GAS DATA FOR SCT (n = 11) AND CONTROLS (n = 12) DURING EXPOSURE TO SIMULATED SEA LEVEL AND AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000m.
- - THE DATA AT BASELINE, PEAK, AND POST EXERCISE FOR BOTH SSL AND S4000M ARE EXPRESSED AS $\bar{X} \pm$ SEM.
- - NO STATISTICALLY SIGNIFICANT DIFFERENCES WERE NOTED BETWEEN GROUPS FOR PvO_2, $Sv0_2$ (%), AND pH.
- - AT SSL, ACUTE STRENUOUS EXERCISE PRODUCED A SMALL AND NOT STATISTICALLY SIGNIFICANT INCREASE IN %S.
- - IN CONTRAST TO EXERCISE AT SSL, A SIGNIFICANT INCREASE IN % SICKLING WITH EXERCISE AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000m WAS OBSERVED.
- - AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000m, %S AT REST INCREASED SIGNIFICANTLY COMPARED TO SSL WHEN (n = 27).
  F_IO_2 24% %SR (0.6$\pm$.16) RANGE (0.2 - 3.8%) (n = 27)
  F_IO_2 14% %SR (1.6$\pm$0.4) RANGE (0 - 9.7%) (n = 27)
- - AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000m, %S WHEN MEASURED AT REST, AT PEAK, AND AT POST PEAK WAS INCREASED SIGNIFICANTLY COMPARED TO SSL IN n = 11 SCT.
- - THE INCREASE IN %S OBSERVED AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000m COMPARED TO SLL PARALLELED THE SIGNIFICANT REDUCTION IN S_VO_2 FOR THE GROUP.

% SICKLING IN ASYMPTOMATIC SCT VOLUNTEERS

		F_IO_2 = 24% (Simulated Sea Level)				F_IO_2= 14% (Simulated 4000m)			
Subject	HbS	%S Rest	%S Peak	%S Post	VO_2/kg	%S Rest	%S Peak	%S Post	VO_2/kg
1	37.7	0.2			42	0.5			28
2	41.1	0.2			46	1.8			34
3	41.6	0.3			53	1.0			36
4	43.4	2.2			40	3.1			28
5	41.9	0.2	0	0	39	0.2	1.9	0.7	30
6	40.6	0.1			45	0.3	4.0	0	34
7	37.6	0.1	0.1		39	0	6.2	10.6	36
8	43.0	0.3	0.9	0.6	58	1.7	25.8	24.0	41
9	42.2	0.8	0	0	47	2.2	6.1	12.2	38
10	38.8	0.7	2.8	0.4	50	1.1	7.6	0.4	36
11	39.2				39	0.7	0	0.3	33
12	36.0	0	2.3	2.0	41	0.3	21.6	27.8	32
13	39.0	0	0	0	46	0	0.7	1.3	34
14	37.9	0			42	0			28
15	40.5	0			35	0.2			29
16	37.4	0.6			46	1.4			31
17	40.3	0			44	1.0			35
MEAN	39.9	0.4	0.9	0.5	44	0.9	8.2	9.5	33
± SEM	± 0.5	± 0.1	± 0.4	± 0.3	±1.4	± 0.2	± 3.1	± 3.8	0.9

% SICKLING IN ASYMPTOMATIC SCT VOLUNTEERS

- - THIS TABLE DEMONSTRATES THE INDIVIDUAL DATA %S IN ASYMPTOMATIC SCT VOLUNTEERS AT SSL AND DURING EXPOSURE TO INSPIRATORY HYPOXIA EQUIVALENT TO 4000m IN THE 17 ASYMPTOMATIC SCT VOLUNTEERS.
- - THE ASYMPTOMATIC MEAN GROUP DATA APPEARS AT THE BOTTOM OF THE SLIDE.
- - %S AT REST AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000m WAS OF BORDERLINE SIGNIFICANCE IN DISTINGUISHING BETWEEN SYMPTOMATIC AND ASYMPTOMATIC SCT VOLUNTEERS.
- - %S OBSERVED DURING EXERCISE AT SSL FOR THE ASYMPTOMATIC GROUP WAS NOT SIGNIFICANTLY DIFFERENT FROM THAT OBSERVED AT SSL FOR THE SYMPTOMATIC SCT GROUP.
- - %S OBSERVED DURING EXERCISE AT SSL COULD NOT PREDICT %S WITH EXERCISE AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000m.
- - ALTHOUGH MEAN VALUES AT S4000m FOR %S AT REST, AT PEAK, AND AT POST WERE HIGHER FOR THE SYMPTOMATIC SCT GROUP COMPARED TO THE ASYMPTOMATIC GROUP, THE HIGHEST LEVEL OF INDIVIDUAL SICKLING WERE SEEN IN THE ASYMPTOMATIC GROUP.

% SICKLING IN SYMPTOMATIC SCT VOLUNTEERS

		F_IO_2 = 24% (Simulated Sea Level)				F_IO_2 = 14% (Simulated 4000m)				
Subject	HbS	%S Rest	%S Peak	%S Post	$\dot{V}O_2$/kg	%S Rest	%S Peak	%S Post	$\dot{V}O_2$/kg	Symptom
1	35.8	0.1			52	0.4			37	Chest pain, leg cramps
2	41.6	0.2				1.2			33	Side Ache-5'
3	41.4	3.8			43	9.7	6.4	10.0	40	LUQ Pain
4	43.8	0.3			51	3.2			34	Stomach cramps
5	40.6	1.1	1.3	0.3	38	3.3	8.9	16.1	28	LUQ Pain
6	41.3	0.8	0.2	0.2	49	0.7	9.4	9.9	30	Leg cramps
7	37.1	0.1			43	0.3			37	Leg cramps
8	41.8	1.3			47	2.2			32	LUQ Pain
9*	43.0				41				33	D, H.A., N; Unstable
10*	43.1	1.8	1.1	2.7	44					D, H.A., N
11*	38.3	0.1			42	1.2				D, H.A., N
12	40.1	1.0			48	6.7			30	Dizzy
MEAN	40.6	1.0	0.9	1.1	45	2.9	8.2	12.0	33	
± SEM	± 0.7	± 0.3			±1.3	± 1.0			± 1.2	

*Unable to exercise at 14%

% SICKLING IN SYMPTOMATIC SCT VOLUNTEERS

- - THIS TABLE INDICATES THE AVAILABLE INDIVIDUAL SICKLING DATA AT SSL AND DURING EXPOSURE TO INSPIRATORY HYPOXIA EQUIVALENT TO 4000m IN THE 12 INDIVIDUALS WITH SCT WHO WERE SYMPTOMATIC.
- - THE SYMPTOMATIC GROUP MEAN DATA APPEARS AT THE BOTTOM OF THE PAGE.
- - % S AT SSL IN THE SYMPTOMATIC GROUP WAS NOT STATISTICALLY DIFFERENT FROM THE TOTAL SCT (n = 27) GROUP AT SSL.
- - % S AT REST AT S4000m WAS SIGNIFICANTLY HIGHER THAN REST AT SSL FOR THE SYMPTOMATIC GROUP. THE % SR AT 14% FOR THE SYMPTOMATIC GROUP WAS STATISTICALLY GREATER FOR THE SCT (n = 27) GROUP 2.9 VS. (1.6 $\pm$ 0.4).
- - % S DURING EXERCISE AT SSL COULD NOT PREDICT %S AT S4000; HOWEVER, n VALUE IS VERY SMALL.
- - INSPIRATORY HYPOXIA EQUIVALENT TO 4000m SIGNIFICANTLY POTENTIATED THE INCREASE IN % S OBSERVED DURING SSL.
- - FURTHER STATISTICAL ANALYSIS IS NECESSARY IN ORDER TO CORRELATE % SICKLING WITH CLINICAL SYMPTOMS.

$\bar{X} \pm$ SEM

F_IO_2 24% %SR (0.6$\pm$ 0.16) RANGE (9.2-3.8%) (n = 27)

F_IO_2 14% %SR (1.6$\pm$ 0.4) RANGE (0-9.7%) (n = 27)

CARDIOPULMONARY PERFORMANCE OF SYMPTOMATIC AND ASYMPTOMATIC SCT VOLUNTEERS

(mean ± SEM)

	F_IO_2 = 24% (Sim. Sea Level)		F_IO_2 = 14% (Sim. 4000 m)	
	SYMPT	ASYMPT	SYMPT	ASYMPT
Peak Power	248±8	257±10	202±9	206±8
Peak $\dot{V}O_2$ (L/min)	3.27±.13	3.26±.12	2.47±.09	2.45±.08
Peak $\dot{V}O_2$/kg (ml/kg/min)	45.3±1.3	44.1±1.4	33.4±1.2	33.2±0.9
Peak HR (bpm)	192±3	193±3	186±3	184±2
AT ($\dot{V}O_2$, L/min)	1.81±.11	1.71±.10	1.49±.07	1.40±.07
PaO_2 (mmHg) Final SS	94±2.0	96±1.7	42±1.0	43±1.1
P (A-a)O_2 (mmHg) Final SS	20±2.1	21±2.0	19±0.7	20±1.3
V_D/V_T (%) Final SS	15±1.1	16±1.0	21±1.0	22±1.1

*Significant difference between groups at $p < 0.05$.

CORRELATIONS OF HbS AND % SICKLING WITH
EXERCISE PERFORMANCE IN SCT INDIVIDUALS

	HbS			%S Baseline			%S Peak		
	n	r	p	n	r	p	n	r	p
				SIMULATED SEA LEVEL					
Power Peak	25	-0.06	>0.1	24	-0.19	>0.1	9	-0.11	>0.1
$\dot{V}O_2$ Peak	25	-0.06	>0.1	24	-0.27	>0.1	9	0.15	>0.1
HR Peak	25	0.27	>0.1	24	-0.03	>0.1	9	0.62	<*0.05
AT	25	0.01	>0.1	24	-0.15	>0.1	9	0.12	>0.1
				SIMULATED 4000m					
Power Peak	25	-0.23	>0.1	25	-0.24	>0.1	9	0.08	>0.1
$\dot{V}O_2$ Peak	25	-0.23	>0.1	25	-0.23	>0.1	9	0.09	>0.1
HR Peak	25	0.06	>0.1	25	-0.21	>0.1	9	-0.12	>0.1
AT	25	-0.05	>0.1	25	-0.18	>0.1	9	-0.30	>0.1

HBS, %S CORRELATION WITH EXERCISE

- - THIS TABLE DEMONSTRATES THE CORRELATIONS OF HBS AND %S WITH PARAMETERS OF EXERCISE PERFORMANCE IN SCT INDIVIDUALS.
- - - %HBS, %S BASELINE VALUES, AND %S PEAK VALUES AT BOTH SIMULATED SEA LEVEL AND DURING EXPOSURE TO INSPIRATORY HYPOXIA EQUIVALENT TO 4000m ARE CORRELATED WITH PEAK POWER, PEAK VO2, PEAK HR, AND ANAEROBIC THRESHOLD.
- - CONSISTENT WITH OUR PREVIOUS DATA, NEITHER %HBS NOR %S CORRELATED WITH PARAMETERS OF EXERCISE PERFORMANCE AT SIMULATED SEA LEVEL AND S4000m.

PERCENT SICKLING (%)

A) AT SIMULATED SEA LEVEL, ACUTE STRENUOUS EXERCISE PRODUCED A SMALL AND NOT STATISTICALLY SIGNIFICANT INCREASE IN % SICKLING.

B) AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m, %S AT REST INCREASED SIGNIFICANTLY COMPARED TO SIMULATED SEA LEVEL.

C) THE LEVEL OF %S AT REST, AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m, WAS OF BORDERLINE SIGNIFICANCE IN DISTINGUISHING BETWEEN SYMPTOMATIC AND ASYMPTOMATIC SCT VOLUNTEERS.

D) IN CONTRAST TO EXERCISE AT SIMULATED SEA LEVEL, A SIGNIFICANT INCREASE IN %S WITH EXERCISE AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m WAS OBSERVED.

E) THE %S OBSERVED DURING EXERCISE AT SIMULATED SEA LEVEL COULD NOT PREDICT %S WITH EXERCISE AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m.

SUMMARY

1) DISCERNABLE CLINICAL DIFFERENCES WERE NOTED BETWEEN THE 2 GROUPS AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m AT REST AND DURING EXERCISE.

2) OVERALL EXERCISE PERFORMANCE WAS COMPARABLE FOR INDIVIDUALS FROM THE SCT GROUP WHO WERE ABLE TO EXERCISE AND THE CONTROL GROUP AT SIMULATED SEA LEVEL AND DURING INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m.

3) IN ADDITION, OTHER SUBTLE PHYSIOLOGICAL PARAMETERS OF CARDIOPULMONARY AND GAS EXCHANGE RESPONSE WHICH INCLUDED P_aO_2, $P(A-a)O_2$, V_D/V_T, AND R WERE ALSO COMPARABLE FOR BOTH GROUPS.

4) DESPITE NORMAL EXERCISE PERFORMANCE, SIGNIFICANT CLINICAL SYMPTOMS WERE STILL NOTED IN SOME SCT VOLUNTEERS.

5) THE NON-SPECIFIC SYMPTOMS RESPONSIBLE FOR 3 INDIVIDUALS WITH SCT BEING CLINICALLY PRECLUDED FROM EXERCISE TESTING ARE OF UNCERTAIN ETIOLOGY.

6) THE DECREMENT IN EXERCISE PERFORMANCE AT A LEVEL OF INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m WAS COMPARABLE FOR BOTH GROUPS.

7) NEITHER %HBS NOR % SICKLING IN SCT VOLUNTEERS CORRELATED WITH PARAMETERS OF EXERCISE PERFORMANCE MEASURED DURING ACUTE STRENUOS EXERCISE UNDER BOTH EXPERIMENTAL CONDITIONS.

CONCLUSIONS

1) THIS STUDY SUGGESTS THAT SOME INDIVIDUALS WITH SCT ARE MORE SUSCEPTIBLE TO CLINICAL PROBLEMS DURING EXPOSURE TO INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m.

2) NO PHYSIOLOGIC PARAMETER CLEARLY DISTINGUISHES INDIVIDUALS WITH SCT WHO ARE MORE LIKELY TO EXPERIENCE CLINICAL SYMPTOMS DURING EXERCISE AND/OR EXPOSURE TO INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m THAN THOSE WHO ARE ASYMPTOMATIC.

3) THE CARDIOPULMONARY RESPONSE TO ACUTE STRENUOUS EXERCISE FOR INDIVIDUALS WITH SCT WHO WERE ABLE TO EXERCISE (MAJORITY) IS INDISTINGUISHABLE FROM CONTROLS UNDER BOTH EXPERIMENTAL CONDITIONS.

4) INSPIRATORY HYPOXIA EQUIVALENT TO 4000 m SIGNIFICANTLY POTENTIATES THE EXERCISE INDUCED INCREASE IN %S MEASURED IN PERIPHERAL VENOUS BLOOD. HOWEVER, %S BY ITSELF DOES NOT APPREAR TO PLAY A CRITICAL ROLE IN THE MODULATION OF EXERCISE PERFORMANCE UNDER THE EXPERIMENTAL CONDITIONS OF THE PRESENT STUDY.

5) %HBS DID NOT CORRELATE WITH PARAMETERS OF EXERCISE PERFORMANCE UNDER BOTH EXPERIMENTAL CONDITIONS.

6) THIS STUDY SUGGESTS THAT BECAUSE OF THE COMPLEX INTERACTION OF MULTIPLE FACTORS INVOLVED IN SICKLING IN VIVO, THAT CAUTION BE EXERCISED IN EXTRAPOLATING IN VITRO SICKLING RESULTS TO CLINICAL SITUATIONS.

7) IN VIEW OF THE REMOVAL OF OCCUPATIONAL DISQUALIFICATIONS FOR ACTIVE DUTY MILITARY WITH SICKLE CELL TRAIT, THE RESULTS OF THE PRESENT STUDY STRONGLY SUGGEST THAT ADDITIONAL CLINICAL STUDIES EVALUATING ADVERSE ENVIRONMENTAL RISK FACTORS ARE WARRANTED.

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GLOSSARY

AT($\dot{V}O_2$, L/min)	Anaerobic threshold
aBGS	Arterial blood gases
DL_{CO} (ml/min/mmHg)	Diffusing capacity for carbon monoxide
DL/V_A (ml/min/mmHg/L)	Diffusing capacity for carbon monoxide per liter of alveolar volume
2,3 DPG	2,3 diphosphoglycerate
F_IO_2(%)	Fraction of inspired oxygen
FVC(L)	Forced vital capacity
FEV_1(L)	Forced expiratory volume in one second
f	Respiratory frequency
FRC	Functional residual capacity
HbS(%major Hb)	Hemoglobin S
HR(bpm)	Heart rate
IET	Incremental exercise test
O_2 pulse (ml/beat)	Oxygen pulse
P_B (mmHg)	Barometric pressure
P_IO_2 (mmHg)	Partial pressure of inspired oxygen
P_{50}	Oxygen tension at 50 percent of Hb saturation
PaO_2 (mmHg)	Arterial oxygen tension
$PaCO_2$ (mmHg)	Arterial carbon dioxide tension
$P(A-a)O_2$ (mmHg)	Alveolar-arterial oxygen pressure difference
PvO_2	Venous oxygen tension
$PvCO_2$	Venous carbon dioxide tension
pH	Negative logarythm of the concentration of free hydrogen ions in solutioin
R	Respiratory exchange ratio
SaO_2 (%)	Arterial oxygen saturation
SvO_2	Venous oxygen saturation
SS	Steady state exercise test
SSI	Level 1 of steady state exercise
SSII	Level 2 of steady state exercise
SSIII	Level 3 of steady state exercise
SSL	Simulated sea level
S4000	Simulated 4000m
TLC(L)	Total lung capacity
$\dot{V}_E$(L/min)	Minute ventilation
V_T	Tidal volume
V_A(L)	Alveolar volume
V_D/V_T(%)	Physiologic dead space to tidal volume ratio
$\dot{V}O_2$(L/min)	Oxygen consumption per minute
$\dot{V}CO_2$(L/min)	Carbon dioxide production per minute
vBGS	Venous blood gases
W (joules/sec)	Watt

LIST OF PUBLICATIONS

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